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Efficacy of Gene Delivery and Expression of Transgenic Stem and Dendritic Cells Using SPECT

Ali Rad[1], Branislava Janic[1], Asm Iskander[1], Mohammad Siadat[1], Ali Arbab[1] and Hamid Soltanian-Zadeh[1]

[1] Radiology, HFHS, Detroit, Michigan

Objectives: Gene therapy holds enormous potential as a therapeutic approach for breast cancer treatment. Several factors, including lack of an efficient vector and delivery system itself, limit the effectiveness of systemically or locally administered genes. Previously, we have shown possible application of endothelial stem/progenitor cells (EPCs) or dendritic cells (DCs) as gene delivery vehicles. In this study, we compared the efficacy of gene delivery of these two cell types at 2 different time points.

Methods: Three million human breast cancer (MDA-MB-231) cells were subcutaneously implanted in the right flank of nude mice. Both, EPCs and DCs were genetically transformed to carry hNIS gene using adenoviral vectors. Genetically transformed cells were administered intravenously in tumor bearing mice. Single photon emission computed tomography (SPECT) images were acquired 3 and 7 days after cell injection, with a custom built micro-SPECT using Tc-99m. Ratio of the total radioactivity of the given tumor volume and the total activity of the same volume on the contra-lateral muscle was used as an indicator of the level of transgene expression.

Results: No difference was observed between EPCs and DCs in their abilities to express and deliver transgenes. In addition, no difference was observed between transgene expression for day 3 and day 7 within the same cell type group. However, histology analysis revealed the pattern of tissue distribution was different for these 2 cell types.

Conclusions: Our study indicates that both EPCs and DCs can be used for gene delivery by systemic administration and their gene expression doesn't change after 7 days of injection. Since DCs can be obtained from the patient peripheral blood, these cells are maybe a better choice for the future development of cell based therapies.

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